UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

VB

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/386,709	08/31/99	BRAYDEN	D 99.1081.US

HM12/0205

ELAN HOLDINGS INC
1300 GOULD DRIVE
GAINESVILLE GA 30504

EXAMINER	
GRASER, J	
ART UNIT	**PAPER NUMBER**
1645	10

DATE MAILED: 02/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/386,709	Brayden
Examiner	**Group Art Unit**
Graser, Jennifer	1645

☒ Responsive to communication(s) filed on *Amendment A, 11/15/2000*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-3, 5-9, and 11-20* is/are pending in the application.

Of the above, claim(s) *1-3, 5-9, 11, and 12* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *13-20* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

1. Acknowledgment and entry of the Amendment submitted 11/15/00, Paper No. 9A is made. Claims 1-3, 5-9 and 11-20 are currently pending.

Election/Restriction

2. Newly amended claims 1-3, 5-9 and 11-12 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Applicant has changed the invention recited in claims 1-3, 5-9 and 11-12 from vaccine formulations to methods of making vaccine formulations. Applicant has already received an examination of these claims as vaccines, not methods of production, as well as an examination on methods of immunizing. This method of producing a vaccine would have been restricted from the vaccines and methods of immunizing if these claims were originally presented as follows:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-3, 5-9 and 11-12, drawn to methods for producing a vaccine, classified in class 424, subclass 400.

II. Claims 13-20, drawn to methods of inducing a protective response against B.pertussis, classified in class 424, subclass 253.1.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process of making and process of using the product. The use as claimed cannot be practiced with a materially different product. Since the product is not allowable, restriction is proper between said method of making and method of using. The product claim will be examined along with the elected invention (MPEP § 806.05(I)).

Since applicant has received an action on the merits for the originally presented invention, i.e., vaccines and methods of immunizing using said vaccines, this invention has been constructively elected by original presentation for prosecution on the merits. A method of making a vaccine which includes coacervating an antigen with a biodegradable polymer is an entirely new and different invention then what was previously examined. Accordingly, claims 1-3, 5-9 and 11-12 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shahin (Infect. Immun. 1995. 63(4): 1195-1200) in view of Jones et al (Infect.Immun., 1996, 64(2): 489-494) in further view of O'Hagan et al (US 5,603,960)..

Shanin et al disclose that purified *Bordetella pertussis* antigens, encapsulated in biodegradable poly (DL-lactide-cp-glycolide) (DL-PLG) microspheres are effective vaccines. The reference discloses that microencapsulated pertussis toxoid, filamentous hemagglutinin, and pertactin all retained their immunogenicity when administered parenterally (abstract). It is also disclosed that intranasal administration of these microencapsulated antigens elicited high levels of specific antibody coinciding with protection against infection when these microspheres are administered to the respiratory tract (abstract).

However, Shanin et al do not particularly exemplify the size of their vaccine compositions.

Jones et al teach that fimbriae from *Bordetella pertussis* encapsulated in poly(lactide-co-glycolide) microparticles of a size appropriate for uptake by the immune inductive tissues of the gastrointestinal tract could protect mice from *B.pertussis* respiratory infection upon oral administration (abstract). It is disclosed that the mean diameter of the microparticles was 2.04um, with 90% of microparticles having diameters within the narrow range of 0.8 to 5.3 um (see page 490, Results section). The microparticles were prepared through a solvent extraction technique (top of page 490, column 1). It is further disclosed that analysis of the mechanism of particle uptake by M cells in mouse gut has clearly shown that this is restricted to materials with diameters less than or equal to 10um (page 492, column 2). It is further disclosed that smaller microparticles (1- to 10- um) were more immunogenic than larger particles (20- to 50- um), as the smaller microparticles were rapidly phagocytosed and distributed (page 290, column 1).

However, Jones et al do not particularly exemplify vaccine compositions comprising

nanoparticles of less than 600nm or less than 500nm in size wherein said nanoparticles comprise at least one antigen entrapped or encapsulated.

O'Hagan et al describe methods for producing microparticles useful in the formulation of pharmaceutical compositions. Methods of immunizing mammals against diseases comprising administering to the mammal an effective amount of antigen-containing microparticles. Vaccines comprising a pharmaceutical composition comprising said microparticles are also disclosed. It is disclosed that the preferred average microparticle size is between 200 nm and 200um (column 3, lines 33-34). It is disclosed that when the microparticles are to be orally administered, the preferred size of the microparticles is preferably between 100 nanometers to 10 um in size (column 7, lines 21-23). It is preferred that the microparticles be administered orally (column 3, lines 40-41). It is disclosed that the microparticles are preferably made with a biodegradable polymer (column 4, lines 63-3). The solvent media used in the solvent evaporation method to produce the microparticles is dependent upon the material to be encapsulated (column 4, lines 60-63). The preferred polymer for encapsulating the bioactive material is a polylactide polymer, or particularly a polylactide-co-glycolide polymer (column 5, lines 24-30).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use nanoparticles less than 600nm or less than 500nm in size as taught by O'Hagan, or microparticles less than 5um as taught by Jones, in place of the microparticles used in the methods of Shahin because the prior art specifically discloses that particle uptake by M cells in the mouse gut is restricted to materials with diameters less than or equal to 10um (page 492,

column 2) and that smaller microparticles (1- to 10- um) were more immunogenic than larger particles (20- to 50- um), as the smaller microparticles were rapidly phagocytosed and distributed (page 290, column 1). O'Hagan teaches vaccine compositions comprising microparticles of 100nm to 10 um in size which are made of the same polymers as those used in the methods of Shanin and Jones and uses similar methods to produce the microparticles. Since Jones, who also teaches DL-PLG encapsulated *B.pertussis* antigen as vaccines, specifically teaches that the use of smaller microparticles allows for a more rapid phagocytosis and distribution, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make the particles of Shanin, i.e., less than 500 or 600nm or less than 5um, absent unexpected or unobvious results, because a person of ordinary skill in the art would expect such a microparticle to improve the immune response of the Shanin method. Further, it would have been obvious that both Ptd and filamentous hemagglutinin could be encapsulated together because the person of ordinary skill in the art would expect such a mixture to improve the range of immune response in an additive or cumulative manner. Mulit-component vaccines were well known in the art at the time the invention was made and the addition of more than one *B.pertussis* antigen in the microparticles, particularly when these antigens have already proven to be effective vaccine components individually, would have been obvious.

Response to Applicants' Arguments:

Applicants argue that Jones et al. fails to disclose the coacervation limitation of base claim 7. This argument has been considered but is not deemed persuasive since this claim has been

withdrawn for the reasons set forth above. Applicants also argue that Jones et al. only discloses the use of fimbriae as a *B.pertussis* antigen while the claim has now been amended so that the vaccine of the method contains at least one antigen consisting of inactivated pertussis toxin (Ptd), filamentous hemagglutinin (FHA) and pertactin. This article has been considered but is rendered moot due to the new grounds of rejection.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Jennifer Graser 2/2/01

Jennifer Graser
Primary Examiner
Art Unit 1645